

REMARKS/ARGUMENTS

Claims 12, 14 to 21, 24 to 28, 30 and 32 are pending in the application. Claims 12, 24, and 27 have been amended herein. No new claims have been added, and no claims have been canceled.

Applicants respectfully request reconsideration of the rejections of record in view of the foregoing amendments and the following remarks.

I. Alleged Indefiniteness

A. Claim 20 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for recitation of the phrase “substantially free of endotoxin.” The Office Action asserts that the phrase is a relative term that renders the claim indefinite. Applicants respectfully traverse the rejection because those of ordinary skill in the art would readily understand the scope of the claimed subject matter when the claims are read in light of the specification.

“If the claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and *if the language is as precise as the subject matter permits*, the courts can demand no more.” *Shatterproof Glass Corp. v. Libbey-Owens Ford Co.*, 758 F.2d 613, 624 (Fed. Cir. 1985)(emphasis added). “[An examiner] should allow claims which define the patentable novelty with a *reasonable* degree of particularity and distinctness. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire.” *Andrew Corp. v. Gabriel Electronics, Inc.*, 847 F.2d 819, 822 (Fed. Cir. 1988)(quoting M.P.E.P. § 706.03(d))(emphasis in original).

The phrase “substantially equal” has at least twice been held by the Federal Circuit to be definite because, even though the phrase is one of degree, it was as precise as the subject matter permitted, and reasonably apprised those skilled in the art of the scope of the claims when read in light of the specification. *See Andrew Corp. v. Gabriel Electronics, Inc.*, 847 F.2d 819, 822 (Fed. Cir. 1988) and *Seattle Box Company, Inc. v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 826 (Fed. Cir. 1984).

As in *Andrew* and *Seattle Box*, the phrase “substantially free of endotoxin” is as precise as the subject matter permits, and apprises those of ordinary skill in the art of the scope of the claimed subject matter when read in light of the specification. Definiteness of claim language must not be analyzed in a vacuum, but in light of the content of the particular application disclosure, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. *In re Moore*, 439 F.2d 1232, 1235 (C.C.P.A. 1971); M.P.E.P. § 2173.02. When the present claim language is so examined, it is apparent that the meaning of the phrase “substantially free of endotoxin” would be readily understood by those of ordinary skill in the art. The specification states that the purity of the alginate used in the claimed compositions and methods is critical, and one advantage of the alginate matrices defined by the claims is that they may be “produced in a high-purity quality having a well defined constitution and a very low content of impurities such as endotoxins.” See page 10, lines 26 to 28. Accordingly, when the phrase “substantially free of endotoxin” is read in light of the specification, those of ordinary skill in the art would readily understand the scope of what is being claimed. The requirements of 35 U.S.C. § 112, second paragraph, have therefore been fulfilled.

Although the Office Action asserts that “[w]ithout a clear definition of the phrase ‘substantially free of endotoxin’, one of ordinary skill in the art would not reasonably be able to determine the metes and bounds of the claim (i.e. what degree or [*sic*] toxin-free would be considered ‘substantially free of toxin’),” as previously discussed, the Federal Circuit has twice held that a precise definition of a phrase of degree, such as “substantially equal” is not necessary or required to apprise those of ordinary skill in the art of the scope of the claimed subject matter. Claims are interpreted in light of the disclosure, teachings in the art, and the knowledge and understanding of those of ordinary skill. When the phrase “substantially free of endotoxin” is thus examined, it is apparent that those of ordinary skill in the art would understand its meaning. Accordingly, Applicants respectfully request withdrawal of the rejection.

B. Claim 24 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly incomplete for omitting essential steps. Specifically, the Office Action asserts that the claim fails to set forth what the claimed one-step procedure comprises. Claim 24 has also been rejected under 35 U.S.C. § 112, first paragraph, because those of ordinary skill in the art would allegedly not know how to perform the claimed method because of its alleged omission of essential steps. Without conceding the correctness of the rejections, and to advance prosecution, claim 24 has been amended to recite a method of producing the composition according to claim 12 comprising introducing a mixture of the producer cells and the alginate into a solution containing multivalent cations. Support for the amendment is found in the specification as filed at, for example, page 11, lines 13 to 27. The rejections have been obviated, and Applicants respectfully request withdrawal thereof.

II. Alleged Lack of Enablement

Claims 27, 28, and 30 have been rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The Office Action asserts that the specification is enabling for methods for treating mammalian patients afflicted with a CNS tumor (or brain tumor) comprising the step of directly administering to the CNS tumor (or brain tumor) an effective amount of the pharmaceutical composition of claim 26 so as to inhibit the growth of said tumor, but does not otherwise reasonably provide enablement for the claimed subject matter. Without conceding the correctness of the assertion, and to advance prosecution, claim 27 has been amended to recite the step of directly administering to the CNS tumor or the site of tumor resection an amount of the pharmaceutical composition according to claim 26 effective to inhibit the growth or regrowth of the tumor. Support for the amendment is found in the specification as filed at, for example, page 5, lines 16 to 20. The rejection has been obviated, and Applicants respectfully request withdrawal thereof.

III. Alleged Obviousness

Claims 12, 14 to 21, 24 to 28, 30, and 32 have been rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over PCT Application No. WO 97/38707 (hereinafter "the Aebischer application") in view of U.S. Patent No. 5,854,205 (hereinafter "the O'Reilly patent") and U.S. Patent No. 5,459,054 (hereinafter "the Skjak-Brek patent"). Applicants respectfully traverse the rejection because the Office Action fails to provide objective evidence that those of ordinary skill in the art would have been motivated to combine the teachings of the cited references, and fails to establish *prima facie* obviousness.

Preliminarily, Applicants note that claim 12 has been amended to recite a composition comprising a producer cell that expresses a molecule that is an inhibitor of the growth of a **malignant** CNS tumor. Support for the amendment is found in the specification as filed at, for example, page 33, line 14 to page 34, line 7 and page 39, lines 14 to 25.

The Office Action fails to identify any credible evidence of a motivation, teaching, or suggestion that would have led persons of ordinary skill in the art, who did not have the benefit of the hindsight provided by Applicants' disclosure, to combine the teachings of the Aebischer application with those of the O'Reilly patent and the Skjak-Brek patent. The Federal Circuit recently reiterated the prohibition against the use of a patent specification as a template for piecing together teachings from multiple references in support of an obviousness rejection, stating that "[i]t is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to 'use that which the inventor taught against its teacher.'" *In re Lee*, 61 U.S.P.Q.2d 1430, 1434 (Fed. Cir. 2002)(citing *W.L. Gore v. Garlock, Inc.*, 721 F.2d 1540, 1553 (Fed. Cir. 1983)). **Objective evidence** of a teaching, motivation or suggestion to select and combine references **must be made of record** by the Patent Office to properly establish *prima facie* obviousness. *Id.* at 1433.

None of the cited references contains a disclosure, teaching, or suggestion that would have led to their combination. Although the Aebischer application describes implantation of encapsulated cells that express an apoptosis-inducing molecule into the CNS, it fails to teach, disclose, or suggest encapsulation of cells that produce endostatin. The O'Reilly patent fails to teach, disclose, or suggest that endostatin is an inhibitor of the growth of **malignant CNS tumors** and fails to teach or suggest that endostatin may be used to treat malignant CNS tumors. The O'Reilly patent describes a protein that is an inhibitor of endothelial cell

proliferation, named endostatin. The patent states that endostatin is an angiogenesis inhibitor, and states that the protein may be used to treat, *inter alia*, “**benign** tumors, for example...acoustic neuromas, neurofibromas.” See col. 10, lns. 43-44 (emphasis added). The O’Reilly patent fails to teach or suggest alginate encapsulation of cells expressing endostatin for the treatment of malignant CNS tumors. The Skjak-Brek patent describes alginate-encapsulated cells, but does not teach, disclose, or suggest encapsulated cells that express a non-endogenous protein, much less encapsulated cells that express endostatin. Accordingly, none of the Aebischer application, the O’Reilly patent, or the Skjak-Brek patent contains a disclosure or suggestion that would have led those of ordinary skill in the art to combine their teachings.

Although the Office Action asserts that those of ordinary skill in the art would have been motivated to combine the teachings of the Aebischer application with those of the O’Reilly patent because “O’Reilly teaches that the nucleic acid encoding endostatin could be used to treat solid tumors and tumor metastases including acoustic neuromas, neurofibromas,” as discussed above, acoustic neuromas and neurofibromas are **benign** tumors, and *the O’Reilly patent does not teach or suggest that endostatin can be used to treat malignant CSN tumors*. Accordingly, those of ordinary skill in the art would not have reasonably expected that endostatin could be successfully used to treat malignant CNS tumors based upon the teachings of the cited references. Those of ordinary skill in the art, therefore, would not have been motivated to combine the references’ teachings.

The Office Action has failed to provide credible, objective evidence of a motivation to combine the teachings of the cited references and has impermissibly used the present claims as a blueprint for piecing together various teachings from the prior art. The Office Action

DOCKET NO.: FMC-1213
Application No.: 09/763,682
Office Action Dated: April 11, 2003

PATENT

has, therefore, failed to properly establish *prima facie* obviousness. Applicants accordingly, respectfully request withdrawal of the rejection.

IV. Information Disclosure Statement

An Information Disclosure Statement and accompanying 1449 Form were filed for the present application on May 11, 2001 and Applicants have not yet received an initialed copy of the 1449 Form. Applicants respectfully ask the Examiner to forward a copy of the initialed 1449 Form to Applicants' undersigned representative, confirming consideration of the listed references.

DOCKET NO.: FMC-1213
Application No.: 09/763,682
Office Action Dated: April 11, 2003

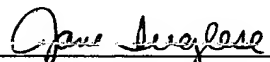
PATENT

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an early and favorable Action is respectfully requested.

Respectfully submitted,

Date:



Jane E. Inglese, Ph.D.
Registration No. 48,444

Woodcock Washburn LLP
One Liberty Place - 46th Floor
Philadelphia PA 19103
Telephone: (215) 568-3100
Facsimile: (215) 568-3439

Please forward all future correspondence relating to this application to:

Patent Administrator
Intellectual Property Law
FMC Corporation
1735 Market St.
Philadelphia, PA 19103